



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,196	09/22/2000	Stephen James Russell	18093/1130	9873
26191	7590	07/06/2005		
FISH & RICHARDSON P.C. PO BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER LUCAS, ZACHARIAH	
			ART UNIT 1648	PAPER NUMBER

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/668,196	RUSSELL ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 April 2005.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-7,9,11-22,24,26,28-30 and 33 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-7,9,11-22,24,26,28-30 and 33 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
     1. Certified copies of the priority documents have been received.  
     2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
     3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>4-29-05</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 1-7, 9, 11-22, 24, 26, 28-30, and 33 are pending and under consideration in the present action. The claims were rejected in the Final action mailed on June 3, 2004. A Notice of Appeal was filed on November 7, 2004, accompanied by an Appeal Brief. An Examiner's Answer was mailed on December 13, 2004.

A request for continued examination (RCE) under 37 CFR 1.114 was filed after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114.

An amendment to the claims (canceling claims 31 and 32) and an information disclosure statement were filed with the RCE, and have been entered into the application.

### ***Information Disclosure Statement***

2. The information disclosure statement (IDS) submitted on April 29, 2005, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

### ***Specification***

3. The disclosure is objected to because of the following informalities:

On page 22, line 22, the specification refers to the use of viable non-infected cells as "controls." It appears that the Applicant intended to refer to the use of the cells as -- controls--.

On page 26, line 11, the application refers to Figure 6B. It appears that the Applicant intended to refer to Figure 5B, as there is no Figure 6B presented in the application.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. (**Prior Rejection- Withdrawn**) Claims 31 and 32 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. In view of the cancellation of these claims, the rejection is withdrawn.

6. (**New Rejection**) Claims 1-7, 9, 11-22, 24, 26, 28, 29, and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods for reducing the number of viable cancer cells in a mammal comprising the administration of Edmonston Measles Virus strains identified in the present application, does not reasonably provide enablement for methods of reducing cancer cells using any attenuated Measles Virus. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, those factors deemed most relevant are the scope of the claims, the presence of working examples, and the state and predictability of the art.

In the present case, the Applicant has claimed methods of administering any attenuated Measles Virus (MV) to a patient in order to reduce the number of viable cancer cells in the patient. In addition to teachings in the art indicating that live Measles virus and plasmids encoding specific MV proteins have been found to either induce the regression of cancers, or to induce cytopathic effects against cancer cells (see e.g., the Taqi and Linardakis references previously cited), the present application has specifically demonstrated the use of certain attenuated strains of MV to induce cytopathic effects in cancer cells. Thus, the combination of the teachings in the art, and in the application are sufficient to demonstrate enablement for the Edmonston strains of attenuated MV disclosed in the application.

As indicated above, the art provides teachings that measles viruses comprise anti-cancer activities. In particular, the art indicates that these activities center around the ability of the F and H proteins of the virus to induce cell fusion (syncytia formation) between cells. See e.g., Bateman et al., Cancer Research 60: 1492-97, esp., pages 1495 and 1496 (teaching that the fusogenic membrane glycoproteins F and H of viruses including the measles virus induce cell fusion leading to the death of cancer cells). However, while the measles viruses are indicated in the art to have anti-cancer capabilities as described above and in the prior actions, certain teachings in the art indicate that this quality is not necessarily present in any attenuated MV.

In particular, attention is drawn to the teachings of Takeda et al. Journal of Virology, 72: 8690-96 (of record in the April 2005 IDS). This reference teaches that three different strains of attenuated MV were unable to induce syncytia formation in infected cells. See e.g., page 8692, second full paragraph; and page 8693, section entitled “Studies with two other pairs of wild-type and Vero cell-adapted strains). See also, page 8692, third full paragraph (suggesting the association of the viral cytopathic effects with its replication and syncytia-forming capabilities). Because the reference teaches that these attenuated virus have no or little syncytial-forming ability, and indicates that such is indicative of no or limited in vivo pathogenicity, the reference provides evidence that these attenuated viruses would not be operable in the claimed methods. Thus, Takeda demonstrates that the ability to induce cell fusion is not inherent to every strain of attenuated MV.

As was indicated above, the art indicates that the anti-cancer activities of MV are based on the ability to induce cell fusion. Such teachings are supported by those of the present application. See e.g., page 6, first full paragraph. However, as exemplified by Takeda, the art

Art Unit: 1648

also teaches that not every attenuated MV is capable of inducing such fusion. Thus, the teachings in the art provide evidence that not every attenuated MV would be useful for the reduction of viable cancer cells.

It is noted that the Takeda reference teaches that each of the attenuated viruses that failed to induce such fusion was attenuated through adaptation for growth in Vero cells. However, the teachings of Johnston et al., (J Virol 73: 6903-15) teach that another strain of attenuated MV adapted for such growth was capable of inducing syncytial formation. See, pages 6904 and 6907 (respectively teaching that 1) the Edmonston attenuated MV strain used in the reference were grown on Vero cells, and 2) that these attenuated MV were capable of inducing syncytia). Johnston also notes the differences between the teachings therein and those of Takeda, and is unable to definitively account for the differences between the activities of viruses in the two references. Pages 6913-14. I.e. the reference indicates that it was not known why one set of attenuated MV was able to induce fusion, whereas the other was not. See also, Bankamp et al., J Virol 76: 7073-81, esp. page 7073, right column, second full paragraph (teaching that it is possible that different unique attenuating mutations are present in different vaccine strains, reference cited in the April 2005 IDS) Thus, rather than resolving the differences between the results in the two references, the Johnston reference highlights uncertainty in the art (i.e. unpredictability) regarding why different MV are, or are not, able to perform the required function. Such uncertainty would also lead those in the art to uncertainty as to which attenuated MV strains would and would not be operative in the claimed methods.

In view of the scope of the art, the limited teachings in the application, the uncertainty in the art, and the demonstration in the art that not every attenuated MV would be capable of operating in the claimed methods, the claims are rejected for exceeding the scope of enablement.

7. **(New Rejection)** Claims 1-7, 9, 11-22, 24, 26, 28, 29, and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The present claims are drawn to a genus of inventions comprising methods of reducing the number of viable cancer cells in a mammal by the administration of any attenuated measles virus.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus.

Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. In the present case, support for the claimed invention may be found by the provision of working examples of the claimed species: i.e., the demonstration of anti-cancer effect in in vitro and animal models by Edmonston strains of MV. Pages 21-26. Thus, the present application provides some written description support for the claimed methods.

However, the courts have also determined that even the presence of multiple species within a claimed genus does not necessarily demonstrate possession of the genus where there is uncertainty in the operation of other species. See e.g., In re Smyth, 178 U.S.P.Q. 279 at 284-85 (CCPA 1973) (stating “where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus or combination claimed at a later date in the prosecution of a patent application.”); and University of California v. Eli Lilly and Co., 43 USPQ2d 1398, at 1405 (Fed Cir 1997)(citing Smyth for support). As indicated above, the present application discloses only the use of a single species. Each of the examples on pages 21-26 of the application concerns the use of only a single (Edmonston) strain of attenuated MV virus. There is no demonstration that this single strain of attenuated MV is representative of all such strains. Rather, the art provides teachings that such is not the case. This is because the teachings of Takeda (described above) indicate that the syncytial-forming and cytopathic capabilities of the Edmonston strain are not common to all attenuated measles viruses.

In view of the disclosure of only a single species, and the uncertainty in the art as to the use of additional species, the application provides insufficient written description support for

Art Unit: 1648

methods of using of any strain of attenuated MV to reduce the number of viable tumor cells in mammals.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. (**Prior Rejection- Withdrawn**) Claims 1-7, 9, 11-17, 20-22, 24, and 28-33 were rejected in the prior action under 35 U.S.C. 103(a) as obvious over Bateman et al (Cancer Research 60:1492-1497- Bateman 2000) in view of Wiebel et al. (Arch. Dis. Childhood 48:532-536 1973), and further in light of the teachings and suggestions of Linardakis (Gene Therapy 6, supp 1, page S4, abstract 13), the Bateman abstract (Gene Therapy 6, supp 1, page S6, abstract 24), Taqi (The Lancet, May 16, 1981, page 1112), Bluming (The Lancet, July 10, 1971, pages 105-06), and Johnston (J Virol 73(8): 6903-15). The Applicant traverses the rejection on the basis that the art provides evidence that attenuated measles virus would not have been understood as interchangeable with the wild-type MV or isolated plasmid DNA based on the teachings of the Takeda et al. reference, described in part above.

In particular, the Applicant asserts that the Takeda reference demonstrates differences between the wild-type and attenuated viruses regarding pathogenicity and the ability to cause cytopathic effects. The reference indicated that attenuated MV, produced through Vero cell

Art Unit: 1648

adaptation, were not pathogenic in vivo, and would thus not have been accepted by the art as usable for the treatment of cancer. The Applicant continues by asserting that the teachings of Takeda would have been appreciated by those in the art as being generally applicable to measles virus attenuation, and that those in the art would therefore have not had a reasonable expectation of success in the use of any attenuated measles virus in the claimed methods.

These arguments are found sufficiently persuasive to overcome the present rejection. This is because the teachings in Takeda are overcome, in part, by the teachings in Johnston. A discussion of the teachings of Takeda and Johnston was presented above. As indicated above, it appears that Takeda would have made those in the art uncertain of the ability of attenuated measles virus in general to operate in the claimed methods. However, contrary to the Applicant's assertion, the teachings would not so much have indicated that no attenuated MV would be operative, as made those in the art uncertain as to what attenuated viruses would or would not be operative. This is because the teachings in the Johnston reference indicate that those of ordinary skill in the art would have had a reasonable expectation of success in the use of the Edmonston strain described therein. The Johnston authors achieved different results from those of Takeda, when using different attenuated MV strains. Their uncertainty as to the source of the different results based on the use of different attenuated virus both supports the Applicant's assertion of uncertainty regarding the use of attenuated viruses in general, but also indicates that those in the art would have expected at least the Edmonston strains to be operative for the treatment of cancers as suggested by the primary references.

However, it is noted that the Weibel reference on which the present rejection is partially based, teaches compositions comprising the Moraten, and not the Edmonston MV strain. The rejection of the claims over this combination of references is therefore withdrawn.

10. **(Prior Rejection- Maintained)** The rejection of claims 1-7, 9, 11-17, 20-22, 24, 26, and 28-33 were rejected in the prior action under 35 U.S.C. 103(a) as obvious over the teachings of Bateman et al. in view of Usonis et al. (Ped Inf Dis J 18:42-48), and further in light of the teachings of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. The rejection is withdrawn from claims 30 and 31, which have been cancelled from the application.

The Applicant traverses this rejection on the same grounds as were asserted with respect to the rejection above. However, it is noted that, in this instance, the Usonis reference teaches the use of an Edmonston strain. In view of the discussion regarding the teachings of Johnston and Takeda above, and the teachings of Usonis, this rejection is maintained.

11. **(Prior Rejection- Maintained in part)** Claims 16 and 17 were rejected in the prior action under 35 U.S.C. 103(a) as obvious over the teachings of Bateman et al. in view of either Weibel or Usonis, and in view of either Asada (Cancer 34: 1907-28, of record in the IDS filed on Jan 5, 2001) or Sato et al (Int J Oral Surg 8:205-11, of record in the IDS filed on July 12, 2002) and further in light of the teachings and suggestions of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. For the reasons indicated above, the rejection is withdrawn to the extent it relies on the Weibel reference to teach the attenuated Measles virus. However, the rejection is

maintained over the rejection to the extent that the Usonis reference is relied upon, in the alternative to Weibel.

12. **(Prior Rejection- Maintained in part)** Claims 18 and 19 were rejected in the prior action under 35 U.S.C. 103(a) as obvious over the teachings of Bateman et al., in view of either Wiebel or Usonis, further in view of Duprex (J Virol 73: 9568-75), and in light of the teachings of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. For the reasons indicated above, the rejection is withdrawn to the extent it relies on the Weibel reference to teach the attenuated Measles virus. However, the rejection is maintained over the rejection to the extent that the Usonis reference is relied upon, in the alternative to Weibel.

13. **(Prior Rejection- Maintained in part)** Claim 20 was rejected in the prior action under 35 U.S.C. 103(a) as obvious over the teachings of either Galanis et al. (Gene Therapy 6 (Supp 1): S7, abstract 28) or Russell et al. (Proc. Am Assoc Cancer Res 41: 259, abstract 1648) in view of either Wiebel or Usonis, and further in light of the teachings of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. For the reasons indicated above, the rejection is withdrawn to the extent it relies on the Weibel reference to teach the attenuated Measles virus. However, the rejection is maintained over the rejection to the extent that the Usonis reference is relied upon, in the alternative to Weibel.

14. **(New Rejection)** Claims 1-7, 9, 11-15, 18-21, 24, 28-30, and 33 are rejected under 35 U.S.C. 103(a) as being obvious over Russell et al. (Russell patent, U.S. 6,896,881). The claims

have been described above. The Russell patent teaches methods of modifying and administering recombinant paramyxoviruses for the treatment of cancers. Abstract. The reference teaches that the virus may be a vaccine strain of a Measles virus, including from the Edmonston and Moraten strains. Column 27, lines 9-28. The reference further teaches the inclusion in the recombinant virus genes encoding the marker protein GFP. Column 27, lines 56-63. Further, the reference teaches that the dosages of the administered virus should be optimized, indicates that the dosage would fall within a range encompassing the claimed dosage amounts, and teaches that the virus may be administered in a single dose, or through repeated doses to the patient or directly to the tumor. Columns 29-30. The reference therefore renders the claimed inventions obvious.

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention “by another”; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

15. **(New Rejection)** Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Russell patent as applied to claims 1-7, 9, 11-15, 18-21, 24, 28-30, and 33 above, and further in view of Usonis and Weibel. These claims read on the methods of the previously described claims, wherein the attenuated MV is administered as part of a compositions also comprising attenuated mumps and rubella viruses. The teachings of the Russell patent have been described above. In addition to the teachings previously described, the Russell patent also indicates that the mumps virus may also be used as the recombinant paramyxovirus used to treat cancer. Column 3, lines 45-47. However, the reference does not teach the administration of such a combined vaccine composition.

The teachings of each of Wiebel and Usonis have been previously described. These references teach that the attenuated measles vaccine strains, respectively, the Moraten and Edmonston strains, are conveniently available to those in the art in safe formulations as combination vaccines with mumps and rubella. As these formulations are known to be safe for human administration, and as the Russell patent indicates that at least 2 of the three attenuated viruses in the composition would be effective in the claimed methods, it would have been obvious to those of ordinary skill in the art to use the compositions disclosed by these reference in the method suggested by the Russell patent. The combined teachings of the references therefore render the claimed inventions obvious.

16. **(New Provisional Rejection)** Claims 1, 18, and 19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

Art Unit: 1648

claim 1 of copending Application No. 11/125,940. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the applications read on overlapping and obvious variants of each other.

The claim of the copending application describe a method of monitoring the reduction in tumor size of a patient comprising the administration of a paramyxovirus to the patient, and measurement of a heterologous polypeptide detectable in the biological fluid of the patient. The specification indicates that a useful paramyxovirus is an attenuated measles virus (page 5). Thus, methods comprising reducing the number of viable cancer cells in a patient represent using an attenuated measles virus represents an obvious variant of the claimed method.

The claims of the present application read on a method of reducing the number of tumor cells in a patient (i.e. reducing the size of a tumor) comprising the administration of a attenuated MV encoding a marker protein. The inclusion of the marker protein is disclosed as useful for the monitoring of the reduction in size of the tumor. App., page 20. Thus, methods of using a heterologous protein to monitor the progression of the claimed cancer treatment represent an obvious variation of the presently claimed methods.

The two applications are therefore claiming obvious variants, each of the other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Conclusion*

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas  
Patent Examiner

PRIMARY EXAMINER  
AL R. SALLI